REMARKS

This document is submitted in response to the Office Action dated April 3, 2006 ("Office Action").

Applicants have amended claim 8 to more particularly point out and distinctly claim the subject matter which they regard as their invention. Support for "analogous activity" and "substantially purified proNGF" can be found, respectively, e.g., at the sentence bridging pages 4 and 5 and at page 20, line 1. No new matter has been added. Of note, Applicants previously withdrew claims 1-7 and 9-19 in view of their response to a restriction requirement and have herein further withdrawn claims 21-25.

Claims 8 and 20 are under examination. Applicants respectfully request the Examiner to reconsider the claims in view of the following remarks.

Rejections under 35 U.S.C. 112, first paragraph (written description)

Both claims 8 and 20 are rejected by the Examiner for failing to meet the written description requirement.

Previously presented claim 8, an independent claim, is drawn to a pharmaceutical preparation containing proNGF as the active ingredient that has activity of a level comparable that of β-NGF.

The Examiner asserts that the Specification does not provide adequate description for the phrase "the proNGF having activity of a level comparable to that of β-NGF." See the Office Action, page 3, lines 10-12.

Applicants have amended claim 8 to recite the phrase "the proNGF having an activity in vivo analogous to β-NGF." The Specification explicitly states that "it has been shown that proNGF has an activity in vivo analogous to B-NGF." See the sentence bridging pages 4 and 5. Applicants therefore submit that amended claim 8 is adequately described.

As claim 20 depends from amended claim 8, it also satisfies the written description requirement for the same reason set forth above.

Rejections under 35 U.S.C. 102(b)

The Examiner maintains that claims 8 and 20 are anticipated by Edwards et al., U.S. Patent 5,683,894 (Edwards), reiterating grounds for rejection from previous office actions. See the Office Action, pages 3-5. Applicants respectfully traverse and will discuss claim 8 first.

I

The Examiner asserts that even a crude preparation of proNGF in a pharmaceutically acceptable carrier can be a pharmaceutical preparation. See the Office Action, page 4, lines 3-6. Applicants disagree.[1] However, in the sole interest of moving this application toward allowance, they have amended claim 8 to recite "a pharmaceutical preparation comprising substantially purified proNGF as the active ingredient." A skilled person would understand that a substantially purified proNGF must be as free as practically feasible of non-proNGF substances. Example 3 of the Specification, at pages 16-20, describes purification of a pro-NGF to the extent permitted by technical and practical constraints.[2] By contrast, Edwards fails to teach or even suggest substantially purified proNGF. As correctly pointed out by the Examiner, Example 4 of Edwards states that "lysates were cleared of particulate material by centrifugation ... in a microcentrifuge to provide a pro-NGF-beta solution" (see the Office Action, page 4, lines 7-8). However, such a solution by no means contains "substantially purified proNGF," as required by amended claim 8, even if it is "no longer [] just a crude preparation" as asserted by the Examiner (see the Office Action, page 4, line 9). The Examiner also refers to the pre-digestion pro-NGF-beta solution prepared in Example 2 of Edwards and used in Examples 5C and 5D of the same reference. See the Office Action, page 4, lines 10-12. That pro-NGF-beta solution, a wheat germ lysate containing in vitro translated proNGF,, was clearly a crude preparation, since particulate material was not even removed from it.

For the reasons set forth above, Applicants submit that the just-mentioned amendment to claim 8 has rendered this claim no longer anticipated by Edwards.

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[1] The term "pharmaceutical preparation," given its ordinary meaning as understood by a skilled person, refers to a preparation that is suitable for administering to a subject to achieve specific therapeutic effect. Thus, a pharmaceutical preparation must contain a certain level of purity to achieve a specific biological result with minimum undesirable side effects. However, according to the Examiner's rationale, any compositions regardless of their purity, including crude cell lysates, are pharmaceutical preparations.

[2] For illustration of a substantially purified proNGF, see Example 4, at pages 21-22, of the Specification.

II

For the sake of a complete record, Applicants address other issues raised by the Examiner in the Office Action as follows:

1. The Examiner asserts that the polyacrylamide gel used in Example 5 of Edwards is a "well known pharmaceutically acceptable excipient for administration ..." See the Office Action, page 4, lines 13-15. Applicants disagree. Although polyacrylamide is not deemed to be toxic, acrylamide, a trace amount of which is often present in polyacrylamide, has been shown to cause cancer and nerve damage. See, e.g., http://www.cfsan.fda.gov/~dms/acryfaq.html and https://fscimage.fishersci.com/msds/89429.htm. The Examiner proceeds to point out that "pharmaceutical carriers are further described in column 10 [of Edwards] (e.g., phosphate buffered saline ...)." See the Office Action, page 4, lines 15-16. Applicants would like to bring to the Examiner's attention that the phosphate buffered saline mentioned in column 10 of Edwards was used as a pharmaceutical carrier for NGF-beta, not for pro-NGF (see, e.g., column 10, line 1). Yet, claim 8 covers a pharmaceutical preparation containing pro-NGF, not NGF-beta, as the active ingredient. Thus, the Examiner's reliance on Edwards's mention of phosphate buffered saline is clearly misplaced. Applicants would like to reiterate that the pharmaceutical preparation of amended claim 8 is distinguishable from all compositions described in Edwards and relied on by the Examiner in that it contains substantially purified pro-NGF. In other words, claim 8 does not base its patentability in use of a unique pharmaceutical carrier.

2. While the Examiner agrees with Applicants that two pro-NGF solutions prepared in Example 6 had little or no NGF-beta activity, he argues that, in view of their structural identity, Edwards's pro-NGF should have the same activity as that of the pro-NGF recited in claim 8. See the Office Action, page 4, last full sentence. The Examiner made the same argument again at page 5, lines 3-13. Applicants would like to point out the possibility that Edwards et al. failed to detect any significant activity of pro-NGF because their pro-NGF preparations were not substantially purified, which is required by amended claim 8. In any event, to maintain this argument, the Examiner has the burden to show that the pro-NGF preparations described in Edwards were actually active, contrary to an explicit statement made in that reference (i.e., column 9, lines 7-9).

3. The Examiner agrees that the Lorey declaration previously submitted by Applicants shows that pro-NGF is active, but notes that enablement should be established at the time of filing. It should be pointed out that, contrary to the Examiner's belief, the Lorey declaration was not submitted to establish that pro-NGF is active, which was already established at the time of filing. See original claim 8 and the sentence bridging pages 4 and 5 of the Specification. Rather, it was submitted to overcome an anticipation rejection, not a lack-of-enablement rejection, by showing that pro-NGF, contrary to the Examiner's belief, indeed had an activity analogous to ß-NGF. See page 7, third paragraph of the response mailed December 29, 2005.

III

Based on the foregoing remarks, Applicants submit that Edwards does not anticipate amended claim 8. As claim 20 depends from amended claim 8, it is also not anticipated by Edwards for the same reasons.

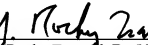
CONCLUSION

Applicants submit that the grounds for rejection stated in this Office Action have been overcome and that the claims under examination satisfy the written description and novelty requirements. Thus, allowance of this application is respectfully requested.

No fee is believed due. Please apply any other charges to deposit account 06-1050.

Respectfully submitted,

Date: 7-3-06



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